REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-69 are in this case. Claims 1-52 and 64 were previously canceled. Claims 53-63 and 65-69 have been rejected.

35 U.S.C. § 102 (b) Rejections

The Examiner has rejected claims 53-55, 63 and 65 under 35 U.S.C. § 102(b) as being anticipated by Rushforth *et al.*, 1989, Abstract No. 223 at 1989 International Worm Meeting. The Examiner's rejections are respectfully traversed.

The Examiner points out that Rushforth *et al.* teach introduction of microinjectiles coated with plasmid DNA into *C. elegans* and recovery of both transient and heritable transformants. The transformants are heritable for many generations which implies that they are stable transformants although the frequency of obtaining heritable transformants is low.

Contrary to Examiner's assertion, the teaching of Rushforth *et al.* do not anticipate the claimed method of the present invention since the targeted organism which is taught by Rushforth *et al.* does not fall within the limitations of claim 53 of the instant application.

The present invention refers to a method of genetically modifying a multicellular eukaryotic diploid parasite. *C. elegans*, on the other hand, is a non-parasitic free living organism. The term "parasite" as defined in the instant application (on page 9 line 38) and as is accepted in the art refers to an organism which, in at least a part of its life cycle, lives on or within another species [from] which it obtains nutrients and/or shelter". Since *C. elegans* is capable of completing its life cycle as a free living organism it is not classified as a parasite according to the instant specification and the art.

Thus, Applicant believes that since the teachings of Rushforth *et al.* do not describe or suggest biolistic transformation of a parasitic organism , and as such, the presently claimed invention is neither anticipated nor rendered obvious by Rushforth *et al.*

35 U.S.C. § 103(a) Rejections

The Examiner has rejected claims 53-63 and 65-69 under 35 U.S.C. § 103(a) as being unpatentable over Miller (WO 97/11191) in view of either Rushforth *et al.*, 1989, Abstract No. 223 at 1989 International Worm Meeting. The Examiner's rejections are respectfully traversed.

In particular, the Examiner points out that Miller *et al.* teach a method of transforming schistosome via microinjection of transgenic DNA into stage I schistosome eggs.

The teaching of Rushforth *et al.* is discussed above with respect to the 35 U.S.C. § 102 (b) Rejection.

The Examiner asserts that it would have been obvious and within the scope of one ordinary skilled in the art at the time the invention was made to substitute the microinjection method as taught by Miller *et al.* with the biollistic bombardment taught by Rushforth *et al.* in order to obtain stable transformation of a diploid parasite, such as a schistosomes, because both schistosomes and *C. elegans* are multicellular parasites and it was well known in the art at the time of the invention to use ballistic bombardment for stable transformation of animal cells and to make genetically modified animals including parasites.

The Examiner further asserts that one having ordinary skill at the time the invention was made would have been motivated to do so in order to use schistosomes as intermediate vector for secretion of a desired protein, such as therapeutic protein, into the bloodstream of humans and other susceptible hosts and to facilitate mass production, quality control, termination of therapy at will and dose titration as taught by Miller *et al.*, or to generate genetically modified *C. elegans* as taught by Rushforth *et al.* with reasonable expectation of success.

As is argued above, Applicant is of the opinion that Rushforth *et al.*, do not describe or suggest transforming a differentiated developmental stage of a parasite and therefore provided no motivation.

Although Miller *et al.* describe transformation of a parasite, such transformation is conducted using microinjection, in spite of the fact that Miller conducted these experiments six years following publication of Rushforth *et al.* The fact that Miller *et al.* preferred using microinjection over biolistic bombardment for

transforming schistosome indicates that the method of Rushforth *et al.* was not accepted or adapted in the art and therefore provided no motivation to an ordinary person skilled in the art to use biolistic bombardment in order to transform a diffentially develpemental stage of multicellular eukaryotic diploid parasites.

Notwithstanding from the above, Applicant is of the opinion that the Examiner was incorrect in asserting that Rushforth *et al.* teach a stable transformation of *C. elegans*. As Rushforth *et al.* admittedly states (see in the Abstract's 3rd paragraph) that "Most of heritable transformants continue to segregate uncoordinated offsprings, indicating that the transforming DNA is likely to be extrachromosomal". Clearly, Rushforth *et al.* failed to achieve stable (genomic) integration of the transgene in *C. elegans*. Thus, the phrase "heritable transformants" as used by Rushforth *et al.* merely refers to extrachromosomal transformants which lose the transgenes they carry, gradually over several generations. Furthermore, although the disclosure of Rushforth *et al.* was published back in 1989, yet no further progress has been reported on successful transformation of *C. elegans*, or even any other related organism, using biolistic bombardment at least not until the time when the present invention was made. The absence of any follow up to Rushforth *et al.* clearly indicates that transforming *C. elegans* or related organisms by biolistic bombardment is not trivial.

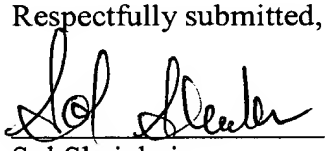
Applicant further wishes to point out that the microinjection method described by Miller *et al.* is ineffective and therefore Miller *et al.* failed to teach one of ordinary skill in the art how to transform schistosomes, as explained in the previous response to Office Action (dated 21 January 2004). Even if the method of Miller *et al.* was effective, the method of the instant application is distinct and substantially advantageous over the method of Miller *et al.*, as explained in great details in the previous response. Applicant, through a detailed and carefully designed experimental set-up which is described in great length in the Examples section of the instant application, developed experimental conditions highly suitable for transforming a differentiated developmental stage of a multicellular eukaryotic diploid parasite, notably schistosomes, via a group transformation method, while preserving its homing and penetration capacity into the hosts, and the development within them.

Therefore, it is the Applicant's opinion that the present application is patentable over the combined teachings of Rushforth *et al.* and Miller *et al.*

In view of the above arguments and claim amendments, Applicant believes to have overcome the 35 U.S.C. § 103(a) rejections.

Therefore it is respectfully submitted that claims 53-63 and 65-69 are now in condition for allowance. Prompt Notice of Allowance is respectfully and earnestly solicited.

Respectfully submitted,



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Date: August 02, 2004.

Encl.:
Two months extension fee.